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| (21) International Application Number: PCT/US99/06271 (22) International Filing Date: 24 March 1999 (24.03.99) (30) Priority Data: 09/047,106 24 March 1998 (24.03.98) US (63) Related by Continuation (CON) or Continuation-in-Part (CIP) to Earlier Application US 09/047,106 (CIP) Filed on 24 March 1998 (24.03.98) (71) Applicant (for all designated States except US): AMWAY CORPORATION [US/US]; 7575 Fulton Street East, Ada, MI 49355 (US). (72) Inventors; and (75) Inventors/Applicants (for US only): GORENBEIN, David [US/US]; Apartment 17J, 1300 Adams Avenue, Costa Mesa, CA 92626 (US). SIDDIQUI, Idrees, A. [IN/US]; 2830 Sheffield Place, Fullerton, CA 92835 (US). CEJA, Ernie, R. [US/US]; 14803 Sabine Drive, La Mirada, CA 90638 (US). HORVATH, Christine, M. [US/US]; 6735 Jennifer Lane, Portland, MI 48875 (US). | (74) Agent: SCHWENNING, Lynn; Amway Corporation, 7575 Fulton Street East, Ada, MI 49355 (US). (81) Designated States: AL, AM, AT, AU (Petty patent), AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DE (Utility model), DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG). Published <i>With international search report.</i> | |
| (54) Title: MULTI-CAROTENOID PRODUCT (57) Abstract <p>A composition is provided that includes carotenoid extracts derived from a plurality of natural sources. Carotenoids are extracted from natural sources such as palm fruit, algae and marigold flowers and combined in a single product. The product contains a broad spectrum of carotenes including alpha-carotene, beta-carotene, Lutein and Zeaxanthin, in amounts that are not typically available from a single natural source. The product may also include carriers such as yellow bees wax, soybean oil and lecithin and may be in a form suitable for oral ingestion.</p> | | |

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MULTI-CAROTENOID PRODUCT

BACKGROUND OF THE INVENTION

Carotenoids are a family of chemical compounds that occur naturally in plants and animals. Non-exhaustive examples of carotenoids are beta-carotene, alpha-carotene, gamma-carotene, lycopene, zeaxanthin, capsanthin and lutein. Each natural source of carotenoids has a distinct array of different carotenoids. For example, it is known that algae contains a mixture of alpha, beta and gamma carotene.

Carotenoids have significant health benefits. For example, beta-carotene is a pre-cursor to Vitamin A, a vital nutrient for human beings and it has been suggested that beta-carotene inhibits heart disease and cancer. Consequently, many people wish to maximize their carotenoid intake. Fruits and vegetables are a desired source of carotenoids because of their nutritional value, cost and availability. Unfortunately, the amount of carotenoids present in natural sources is so small that an inordinate amount of fruits and vegetables would have to be digested to obtain a desired amount of carotenoids.

Thus, methods have been devised to extract and concentrate beta-carotene from various sources. U.S. Patent No. 5,310,554 to Haigh describes a method for making high-purity natural beta-carotene by extracting algae with organic solvents and chromatographing the extract on a column of alumina. U.S. Patent No. 4,680,314 to Nonomura describes a method for purifying beta-carotene by extracting algae with an edible oil.

In addition, several manufacturers have attempted to synthetically manufacture beta-carotene. For example, Hoffmann La Roche, a Swiss pharmaceutical and chemical company, manufactures synthetic all-*trans*-beta-carotene. Synthetic carotenoid compounds, however, almost exclusively contain a specific conformation of a particular carotenoid and contain only trace amounts of other carotenoids or other conformations of the particular carotenoid.

These carotenoid products are either derived synthetically or derived from a single source and fail to provide a balanced supply of carotenoids. Because these products contain a very narrow range of carotenoids, the benefits are

commensurately narrow. Each carotenoid, and individual isomers and conformations thereof, possesses unique and distinctive characteristics and benefits. Not all of the benefits associated with each carotenoid are known or understood. Moreover, the exact amount and type of carotenoids present in the individual sources is not always known. As a result, the known carotenoid products are not able to provide each of the benefits, known and unknown, associated with the many different carotenoids.

Consequently, there is a need for a carotenoid product that is able to provide a comprehensive regimen consisting of a wide variety of different carotenoids.

SUMMARY OF THE INVENTION

In order to provide a comprehensive, effective carotenoid regimen, despite this lack of knowledge of the presence or effect of each carotenoid in a particular natural source, a multi-carotenoid product is provided that includes a plurality of carotenoids, derived from a plurality of sources, in a single product or unit dosage form. Preferably, extracts of palm fruit, algae and marigold flowers are used. Most preferably, these extracts are combined with soybean oil, yellow wax and lecithin in a form suitable for oral ingestion. Surprisingly, the carotenoid product of the present invention is a highly effective and beneficial means to supplement carotenoid intake.

A method of making a multi-carotenoid product is provided where at least one source of alpha-carotene and beta-carotene is combined with at least one source of gamma-carotene, lycopene or lutein.

DESCRIPTION OF THE PREFERRED EMBODIMENT

The multi-carotenoid products of the present invention comprise carotenoid extracts derived from a plurality of sources. In a preferred embodiment there are at least three sources. Preferably, each source is a natural source. The natural carotenoid extracts of the present invention may be derived from any natural source that contains carotenoids. Natural sources are those sources that are organic in composition, such as living things, and are not the result of artificial chemical synthesis. The preferred sources are plants. Non-limiting examples of such sources are marigold flowers, palm fruit, algae (preferably of the class Chlorophyta, more preferably of the genera Dunaliella or Chlorococcus), spinach, broccoli, alfalfa,

tomatoes and carrots. Most preferred are palm fruit, *Dunaliella* algae and marigold flowers.

While it is preferred to use only natural sources of carotenoids, specific carotenoids, or specific conformations of carotenoids, may be supplemented through the use of artificial or synthetic carotenoid products. Synthetic carotenoid products generally consist of a very narrow range of carotenoids and essentially comprise a single conformation of a specific carotenoid. Consequently, the use of synthetic carotenoids is not a desirable means of providing a wide variety of carotenoids; however, the use of synthetic carotenoids is an effective means of providing a very specific amount of a particular carotenoid.

The carotenoids of the present invention may be isolated from their sources by any means available. Preferably, the carotenoids are isolated through solvent extraction. More preferably, the carotenoid extract is further purified through chromatography and/or removal of the extracting solvent. In a most preferred embodiment the carotenoids are extracted with a natural, edible oil to the exclusion of toxic volatile organic compounds. An example of such a process is provided in U.S. Patent No. 4,680,314 to Nonomura, which is incorporated herein by reference in its entirety.

In one embodiment of the invention, the carotenoids may be derived from the following sources: (1) extracted from *Dunaliella* algae with a vegetable oil solvent as described in U.S. Patent No. 4,680,314, and available from Nutrilite Products, Inc. as PROVATENE; (2) extracted from palm fruit oil as described in European Patent Application No. 0 242 148 (which is incorporated herein by reference in its entirety) and manufactured by Quest International under the trade name Caroplex; and (3) extracted from marigold flowers as described in U.S. Patent Nos. 5,382,714 and 5,648,564 (which are incorporated herein by reference in their entirety) and available from Kemin. Preferably, the algal extract is extracted from algae of the class Chlorophyta. In a more preferred embodiment, the algal extract is extracted from ~~algae of the genera *Dunaliella* or *Chlorococcus*~~. An alternative source of *Dunaliella* algae-derived carotenoids is BETATENE from Henkel. This particular mixed carotene material is standardized to contain 200 mg of five naturally occurring carotenoids, namely beta-carotene, alpha-carotene, zeaxanthin, cryptoxanthin, and

lutein. The beta-carotene accounts for 95% of the carotenoids in the BETATENE material.

In a preferred embodiment of the invention, the carotenoids are derived from Dunaliella algae, palm fruit and marigold flowers. Preferably, a supplement in accordance with this invention includes about from about 5 to about 35% of the algal extract, from about 1 to about 10% of the palm fruit extract; and from about 1 to about 5% of the marigold extract. The resulting product contains a broad spectrum of carotenes including alpha-carotene, beta-carotene, Lutein and Zeaxanthin, in amounts that are not typically available from a single natural source.

The multi-carotenoid product of the present invention may include a number of different carriers and/or binders to provide the multi-carotenoid product in a consumable form, e.g., by oral ingestion. The useful and suitable carriers and binders are known to those of skill in the art and are typically neutral, non-toxic additives that facilitate consumption and absorption of the product by the user. Examples of liquid carriers are vegetable oils, such as corn and soybean oil, and mineral oil. Examples of solid carriers and binders are yellow bees wax, glucose, sucrose, starch, lactose, mannitol, magnesium stearate, magnesium carbonate, talcum, and cellulose. Preferably, these ingredients are derived from natural sources. In the preferred embodiment the carrier is a combination of soybean oil, yellow bees wax and lecithin. A supplement made in accordance with this preferred embodiment would include from about 30 to about 60% soybean oil; from about 5 to about 20% yellow bees wax; from about 0 to about 10% lecithin; from about 5 to about 35% of the algal extract; from about 1 to about 10% of the palm fruit extract; and from about 1 to about 5% of the marigold extract.

It is preferred to provide the multi-carotenoid product with the carriers and binders described above as a unit dosage in a softgel capsule. Suitable softgel capsules are available from R.P. Scherer, St. Petersburg, Florida.

The relative amounts of the carotenoids and the carrier depends upon the desired carotenoid dose to be administered. Consequently, the carotenoids can comprise from about 0.01 % to about 99.99% by weight of the multi-carotenoid product. Preferably, the carotenoids comprise from about 0.1% to about 25%, more preferably from about 1% to about 5%.

Similarly, the relative amounts of the individual carotenoid sources is highly variable. The amount of each particular carotenoid source in the multi-carotenoid product depends on which particular carotenoid is most desired and upon the concentration of the carotenoids in the sources.

5 A first embodiment of the present invention is detailed in Table 1.

Table 1

| INGREDIENT | WEIGHT % |
|-------------------------|----------|
| Soybean Oil | 49.71 |
| Yellow Bees Wax | 11.03 |
| Algal Extract | 29.41 |
| Lecithin | 4.90 |
| Palm Fruit Extract | 3.43 |
| Marigold Flower Extract | 1.52 |

10 The algal extract comprises about 2.15% beta-carotene and about 0.23% alpha-carotene in a corn oil suspension. The palm fruit extract comprises about 10% alpha-carotene, about 19% beta-carotene, about 0.36% gamma-carotene, and about 0.03% lycopene in vegetable oil. The marigold flower extract comprises about 20% lutein in corn oil suspension and is available from Kemin. The product is packaged in a soft-gel caplet provided by R.P. Scherer. Included in the composition
15 is soybean oil, yellow bees wax and lecithin. These components act as a carrier for the carotenoid extracts and create an easily ingestible product.

In another embodiment of the invention, the supplement contains a total of about 4 mg to about 10 mg of mixed carotenes that have been obtained from the combination of algae, palm fruit, and marigold flower extracts. Preferably, the
20 supplement includes an amount of the provitamin A carotenoids that is sufficient to provide at least 100% of the reference daily intake of Vitamin A. As used herein, a "provitamin A" carotenoid is a carotenoid which is a precursor to a retinoid such as retinol, retinal and retinoic acid, wherein the retinoids are forms of preformed vitamin
A. Generally, only the alpha and beta carotenes function as a provitamin A
25 carotenoid. In a preferred embodiment, the following spectrum of carotenes is provided:

retinol, retinal and retinoic acid, wherein the retinoids are forms of preformed vitamin A. Generally, only the alpha and beta carotenes function as a provitamin A carotenoid. In a preferred embodiment, the following spectrum of carotenes is provided:

5

Table 2

| Carotene | Amount (mg) | Weight % |
|-----------------|--------------------|-----------------|
| Beta | 4.50 | 64.4 |
| Alpha | 1.07 | 17.0 |
| Lutein | 1.12 | 17.8 |
| Zeaxanthin | 0.045 | 0.8 |
| Total | 6.735 | 100% |

10 In the product described above, the beta-carotene provides 150% of the reference daily intake for Vitamin A.

In addition to the above compositions, a method of making comprehensive carotenoid compositions is also highly useful. Sources of carotenoids are selectively chosen to complement one another and create a product having a wide range of carotenoids. For example, a source that has a particularly high concentration of one carotenoid, but lacking in a second carotenoid, would be combined with a source that has a particularly high concentration of the second carotenoid. In a preferred embodiment, at least one source of alpha-carotene and beta-carotene is combined with at least one source of gamma-carotene, lycopene or lutein. It is preferred that the total amount of carotenoids is at least about 2% by weight.

Of course, it should be understood that a wide range of changes and modifications can be made to the embodiments described above. It is intended, therefore, that the foregoing description illustrates rather than limits this invention, and that it is the following claims, including all equivalents, that define this invention.

What is claimed is:

1. A composition comprising carotenoid compounds derived from a plurality of sources.

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2. The composition of claim 1 wherein the sources are natural sources.

3. The composition of claim 1 wherein the sources are selected from the group consisting of marigold flowers, palm fruit, algae, spinach, broccoli, alfalfa, tomatoes and carrots.

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4. The composition of claim 1 wherein the carotenoid compounds are extracted from their sources.

15

5. The composition of claim 1 further comprising pharmaceutical carriers suitable for oral ingestion.

6. The composition of claim 1 further comprising pharmaceutical carriers selected from the group consisting of yellow bees wax, soybean oil, and lecithin.

20

7. A composition comprising:

- a. an algal extract;
- b. a palm fruit extract; and
- c. a marigold flower extract.

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8. The composition of claim 7 wherein the algal extract is extracted from algae of the class Chlorophyta .

9. The composition of claim 7 wherein the algal extract is extracted from algae of the genera Dunaliella or Chlorococcus.

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10. The composition of claim 7 wherein the algal extract is extracted from algae with an edible oil.

11. The composition of claim 7 wherein the palm fruit extract is extracted from palm fruit oil with an organic solvent, chromatographed on a silica or alumina column and resuspended in an edible oil.

12. The composition of claim 7 wherein:

- a. the algal extract is extracted from Dunaliella algae with an edible oil; and
- b. the palm fruit extract is extracted from palm fruit with an organic solvent, chromatographed on a silica or alumina column and resuspended in an edible oil.

13. The composition of claim 7 comprising:

- a. from about 5 to about 35% of the algal extract;
- b. from about 1 to about 10% of the palm fruit extract; and
- c. from about 1 to about 5% of the marigold extract.

14. The composition of claim 7 further comprising:

- a. soybean oil;
- b. yellow bees wax; and
- c. lecithin.

15. The composition of claim 14 comprising:

- a. from about 30 to about 60% soybean oil;
- b. from about 5 to about 20% yellow bees wax;
- c. from about 0 to about 10% lecithin;
- d. from about 5 to about 35% of the algal extract;
- e. from about 1 to about 10% of the palm fruit extract; and
- f. from about 1 to about 5% of the marigold extract.

16. A composition consisting essentially of:

- a. an algal extract;
- b. a palm fruit extract; and
- c. a marigold flower extract.

- 5 17. The composition of claim 16 further including a carrier.
18. The composition of claim 16 consisting essentially of:
- a. from about 30 to about 60% soybean oil;
 - b. from about 5 to about 20% yellow bees wax;
 - 10 c. from about 0 to about 10% lecithin;
 - d. from about 5 to about 35% of the algal extract;
 - e. from about 1 to about 10% of the palm fruit extract; and
 - f. from about 1 to about 5% of the marigold flower extract.
- 15 19. A method of making a multi-carotenoid tablet comprising combining at least one source of alpha-carotene and beta-carotene with at least one source of gamma-carotene, lycopene or lutein.
20. The method of claim 19 wherein the total amount of carotenoids is at
20 least about 2% by weight.
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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/06271

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) : A61K 31/00

US CL : 424/195.1, 439; 514/725, 783, 763, 766; 585/351

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/195.1, 439; 514/725, 783, 763, 766; 585/351

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
none

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, Bioscience

palm oil extract, marigold oil extract, carotenoid, carotene, combination

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-------------|--|---------------------------|
| X - Y | WO 97/47278 A1 (LABORATOIRE OENOBIOL) 18 December 1997 (18-12-97), abstract; page 5, lines 11-34, claim 1. | 1-6, 19 ----- 20 |
| X - Y | WO 96/19217 A1 (HENKEL CORPORATION) 27 June 1996 (27-06-96), page 4, lines 3-8, page 5, lines 1-25. | 1-5, 19 ----- 6, 20 |
| Y | US 5,310,554 A (HAIGH) 10 May 1994, column 3, lines 39-46. | 7-18 |
| Y | US 5,382,714 A (KHACHIK) 17 January 1995, claims 1-4. | 7-18 |

☐ Further documents are listed in the continuation of Box C.☐ See patent family annex.

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Authorized officer

Cybille D. Mulrhead

Telephone No. (703) 308-0196